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Cataract surgery with femtosecond laser versus conventional phacoemulsification in patients with Fuchs' dystrophy

Cirurgia de catarata com laser Femtosegundo versus facoemulsificação convencional em pacientes com distrofia de Fuchs

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KEYWORDS:

Fuchs; FED; Femtosecond; FLACS; Conventional phacoemulsification.

ABSTRACT

Fuchs endothelial dystrophy is the most common form of corneal dystrophy that affects the endothelium and its function. Intraocular surgeries can dramatically worse the patient situation and therefore must always be carefully done. Femtosecond laser-assisted cataract surgery is an alternative technique for cataract surgery in these patients with fragile endothelium when compared to conventional phacoemulsification. The current study present Fuchs Endothelial Dystrophy and reviews the comparation between Femtosecond laser-assisted cataract surgery versus Conventional Phacoemulsification cataract surgery in patients with Fuchs.

PALAVRAS CHAVES:

Fuchs; FED; Femtosegundo; FLACS; Facoemulsificação.

RESUMO

A distrofia endotelial de Fuchs é a distrofia corneana mais comum que acomete o endotélio e sua função. Cirurgias intraoculares podem piorar dramaticamente a situação do paciente e por isso devem sempre ser realizadas com extrema cautela. A cirurgia de catarata com laser Femtosegundo pode ser uma técnica alternativa para pacientes com fragilidade endotelial quando comparado a cirurgia de catarata convencional com facoemulsificação. O presente estudo apresenta a distrofia endotelial de Fuchs e revisa a comparação de cirurgia de catarata com uso do laser Femtosegundo versus a cirurgia tradicional de catarata com facoemulsificação em pacientes com Fuchs.

INTRODUCTION

The first cases of Fuchs' endothelial dystrophy (FED) were described in 1910 by Ernst Fuchs. Slit-lamp biomicroscopy did not exist back then, and the disease was determined to be an epithelial disorder, *dystrophia epithelialis corneae* (Fuchs 1910)[1]. In 1921, Vogt used the term "guttata," which originates from the Latin word for "droplet-shaped"[2].

FED is the most common endothelial corneal dystrophy[2], and its complex pathophysiology can lead to severe loss of endothelial cells over the years. Literature reports that a physiological loss of endothelial cells occurs with age at a rate of 0.6% per year[3]. This loss in cell numbers may increase to a rate of 2.5% per year in patients who have undergone intraocular surgeries, such as cataract surgery[3]. The endothelium of patients with FED undergoing cataract surgery is

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believed to be more damaged than in patients with healthy endothelium[4]. Severe endothelial loss can be challenging for cataract surgeons.

Since the first intraocular lens implant in 1949 by Dr. Harold Ridley at St. Thomas Hospital, cataract surgery is in a state of constant development. Technical and technological advancement increasingly allows the performance of less invasive surgeries with better results. The use of femtosecond lasers in cataract surgery emerged as a promising and possibly advantageous technology, compared with traditional phacoemulsification surgery. The use of this new, less invasive technology could preserve the endothelium better and could benefit patients with endothelial diseases such as FED.

Since 2009, some studies have compared the outcomes of cataract surgeries using femtosecond laser and those of traditional surgery using phacoemulsification. Other studies have also made the same comparison, but specifically in patients with a previous diagnosis of FED. The present article aims to review the studies on this topic.

Fuchs' endothelial dystrophy

FED is a genetically heterogeneous disease with variable expression and incomplete penetrance[2,5]. The disease may have two forms of presentation: early-onset and late-onset, both of which are autosomal dominant; however, each may have specific genetic characteristics that contribute in different ways to the pathophysiology of the disease. The most significant mutation that happens in the more common late-onset form of the disease is repetition of the cytosine-thymine-guanine trinucleotide in an intron of gene transcription factor 4. Patients carrying the expansion of this trinucleotide have been found to be 15-76 times more likely to develop the disease when compared with patients who do not carry this genetic modification[6]. The length of this expansion is positively correlated with the Krachmer clinical scale for FED and also with higher chances of corneal transplantation in younger people[7]. A minority of cases present with mutations in different genes, such as COL8A2, SLC4A11, ZEB1, LOXHD1, and AGBL1[5,7].

Epidemiology shows that the prevalence of FED in Caucasians is higher than that in other races, such as in Asians, for example. A gender disparity also exists, as the gender ratio ranges from 2.5-3 affected women for every affected man. The prevalence of the disease varies widely across literature, and this is probably due to different clinical definitions of cornea guttata[1]. Some studies estimate prevalence values between 4% and 9% after age 50, depending on the region[6,8]. FED is mostly an age-related disease, and most cases occur in patients 40 years of age or older[6,10].

Fuchs' disease has a complex pathophysiology, and studies with an aim to completely understand it are still ongoing. Genetic and environmental predispositions culminate in different mechanisms that play a role in the disease, either individually or in combination. These mechanisms may include ion channel changes, oxidative stress, epithelial-mesenchymal transitions, and apoptosis[2,7,11]. As a result of these changes, endothelial cells begin to degenerate and produce a pathological secretion that creates hyaline excrescences known as guttata, and apoptosis occurs around the guttata[5].

In the early stage, the remaining endothelial cells can compensate for the lost cells by modifying their original shape (polymorphism) and their size (polymegatism)[7]. However, with the progression of the disease, the number and size of the excrescences increase, and they tend to cluster and form confluent guttata. Initially, guttata appear in the center of the cornea, but they gradually spread to the periphery. The endothelial cell count in the periphery has shown to be a better predictor of disease severity than central corneal thickness, the clinical scale, or even visual acuity[5].

In more advanced stages, the endothelium that has adapted around the excrescences appears to be unable to maintain corneal deturgscence, causing an increase in corneal thickness[11]. The light that reaches the cornea can spread upon reaching the guttata and cause a visual deficit even before corneal edema appears[7,12]. The retained fluid is the cause of corneal edema, which can further worsen the patient's vision. Corneal edema is more likely to occur when the density of endothelial cells is less than 1000 cells per square millimeter[2]. Primary dysfunction affects the corneal endothelium, but in more advanced stages, all corneal layers can be affected. This may lead to stromal edema, epithelial bullae, sub-epithelial fibrosis, and loss of the sub-basal nerve layer. Eventually, these epithelial bullae can burst and cause pain[2,6,7,12].

Cataract surgery with femtosecond laser

The concept of cataract surgery with a femtosecond laser was initially proposed in 2009 with the aim of improving the accuracy and safety of this

surgical procedure. The system uses ultrashort laser pulses that increase the energy of the medium and thereby creates plasma of free electrons and ionized molecules. The rapid expansion of this plasma creates cavitation bubbles capable of separating tissues. This phenomenon is called photodisruption[11–13]. The wavelengths used are not absorbed by the cornea and the laser can therefore be targeted at different depths in the anterior chamber without the risk of damaging the corneal tissue[11].

With the aid of the femtosecond laser, fundamental steps, such as corneal incision, anterior capsulotomy, and nucleus fragmentation, can be performed with high accuracy, precision, and reproducibility[14].

Since the introduction of this technology, several studies have compared its results with one of the conventional cataract surgeries, i.e., phacoemulsification. The most frequently compared parameters were visual acuity, refractive results, and complications.

Popovic et al., in a meta-analysis that included 14,567 eyes, found no statistically significant difference between femtosecond laser surgeries and conventional surgeries in terms of postoperative visual acuity (both corrected and uncorrected)[15]. In agreement with Popovic et al., the FEMCAT multicenter study also found no difference between the two groups in terms of visual acuity 3 months after surgery[16]. In 2016, a meta-analysis by Chen X et al. showed a better corrected visual acuity in the femtosecond laser group in the first week after surgery, but this difference did not persist at the end of the first month or at the end of the follow-up period[17].

Some studies have analyzed and compared the complications between the two surgical techniques. The most frequently compared complications were capsule ruptures (both anterior and posterior), postoperative intraocular pressure, corneal thickness, and macular edema due to the proinflammatory state. There was no definite consensus on which technique has fewer complications. Wang et al., for example, showed that the risk of incomplete capsulotomy, tags in the anterior capsule, and anterior capsule rupture was significantly higher in the group that underwent femtosecond laser-aided surgery[17]. Other studies showed higher prostaglandin levels in the femtosecond laser group[15,18]; this could contribute to cystoid macular edema[19]. In contrast, some other studies did not show any significant differences in complication rates between the two assessed groups[15,16,20], leading to a final disagreement on which method was safer.

Femtosecond laser versus conventional surgery in Fuchs' dystrophy

FED occurs predominantly after the fifth decade of life[6,8]. It primarily compromises the Descemet membrane and the corneal endothelium, which may lead to corneal decompensation and loss of vision. In general, cataracts also occur in older ages, especially after 60 years of age. Despite being different entities, in their natural evolution both diseases tend to worsen over time and decrease the patient's visual acuity. Intraocular surgeries, such as cataract surgery, can increase the loss of endothelial cells and, consequently, the severity of FED. Therefore, safer techniques for performing cataract surgeries can possibly be beneficial to patients with this condition. In 2009, the United States Food and Drug Administration approved the use of femtosecond lasers in cataract surgery. Since then, studies have been conducted to compare this new technique with conventional phacoemulsification surgery in patients diagnosed with FED. The objective was to evaluate which method could be more beneficial given the known pre-existing condition of the patient's cornea and its complications.

The most frequently evaluated parameters in literature were corrected visual acuity in the postoperative period and corneal characteristics, such as endothelial cell density, loss of endothelial cells, and central corneal thickness[21–24].

In theory, the use of a femtosecond laser would decrease the time required for ultrasound use because the laser allows steps, such as fragmentation of the core[24,25]. A shorter duration of ultrasound usage in the anterior chamber may decrease biomechanical damage to the cornea and thereby reduce the loss of endothelial cells and corneal edema (Abell et al, 2014). Reducing endothelial cell loss in patients with FED can be beneficial and possibly delay or prevent future complications.

In 2018, Wei Danya YW et al. compared the outcome of patients with FED who underwent conventional cataract surgery with that of patients undergoing femtosecond laser treatment. The cross-sectional study by Wei Danya YW et al. included a sample of 140 eyes and showed a significantly higher preoperative and postoperative difference in the density of endothelial cells in the group undergoing conventional surgery compared with the group treated with the femtosecond laser[24]. In 2018, a prospective controlled study published by Fan W et al. compared the loss of endothelial cells and the central thickness of the cornea in

two groups of patients with FED, one who underwent conventional cataract surgery and the other who underwent femtosecond laser treatment. In agreement with the outcome of the study by Wei Danya et al., there was a greater percent loss of endothelial cells in the conventional surgery group 1, 3, 6 and 12 months after surgery[21]. In a prospective cohort study including only patients with healthy corneas, Abbel et al. reported greater loss of endothelial cells in the third postoperative week in the group of patients undergoing conventional surgery[26]. Other studies did not show any significant difference in the decrease of endothelial density or the number of endothelial cells between the two groups.

It is important to understand that a greater loss of endothelial cells does not necessarily impact corneal thickness, as evidenced by the study by Wei Danya et al. In that study, although the group that underwent conventional surgery obtained a greater difference in the number of endothelial cells before and after surgery, the central corneal thickness remained similar in both the groups. The long-term surgical outcomes, in terms of the central thickness of the cornea, in femtosecond laser-aided surgery were similar to those of conventional surgery [21,22,24].

Even studies showing a better performance of femtosecond laser-aided surgery in terms of endothelial cell density did not show statistically significant differences in central corneal thickness. Thus, the comparison of the final outcome between the two groups did not show which method was safer or better in relation to these corneal parameters when patients with FED needed to undergo cataract surgery.

As mentioned above, in patients with healthy corneas, both surgeries, conventional and femtosecond laser, obtained satisfactory postoperative corrected visual acuity, but neither group was superior to the other. In patients with FED, the outcome was similar: neither group showed better results than the other[21,22,24]. Zhu D et al. conducted a retrospective case series study at the Bascom Palm Eye Institute on 207 eyes with FED that underwent conventional cataract surgery and femtosecond laser-aided surgery. The authors found no significant difference between the two groups in relation to corrected visual acuity in any postoperative consultation. In both the groups, acuity worsened on the first postoperative day, but unlike the group that underwent conventional surgery, there was a persistent worsening in visual acuity in the first week after surgery in the group treated with a femtosecond laser. One month after surgery, no difference was found[21].

Final visual acuity is a very important outcome when two methods of cataract surgery are compared; it may be the most relevant parameter for the patient. Thus, it can help guide the decision of the method of choice. The existing literature proves that both techniques achieve good postoperative corrected visual acuity, but there is no difference in the result between the techniques[21,22,24].

Patients with FED need to be closely assessed and followed up by an ophthalmologist. Special attention should be paid to whether these patients need to undergo intraocular surgery. Cataract surgery is constantly developing and new techniques, such as the femtosecond laser, aim to improve the results and outcomes, although the advantages offered do not always reflect significant final clinical outcomes. The risk of corneal decompensation may depend more on the patient's baseline characteristics, the surgeon's experience, and intraoperative factors[22]. Accurate criteria could help in choosing the better technique for each patient undergoing surgery. However, the clinicians should be aware of the limitations of each technique.

The literature lacks a comparison of conventional cataract surgery with femtosecond laser-aided surgery in patients diagnosed with FED. Studies with higher levels of evidence should be performed for better clarification and confirmation of which surgical technique is better for these patients.

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